

REMARKS/ARGUMENTS

Claim rejections under 35 U.S.C. §102(b):

The Examiner has maintained her rejection of claims 1, 3, and 5 under 35 U.S.C. §102(b) as being anticipated by Greathouse, et al. (U.S. Pat. No. 3,023,144) and by Chastain, et al. (U.S. Pat. No. 5,153,229). For the following reasons, the Applicant respectfully traverses this rejection.

The Examiner argues that Greathouse et al. teaches d-limonene having “low activity but does not state it (limonene) has no activity.” (Examiner’s Action, page 2). The Examiner further points out that the Greathouse reference teaches synergistic activity when d-limonene is combined with other derivatives, further supporting the Examiner’s argument that “d-limonene played an active part in the fungicidal and bacteriocidal action . . .” (Examiner’s Action, page 3). The Applicant respectfully disagrees with the Examiner’s characterization of this reference, for on the contrary, Greathouse, et al. does not teach any therapeutically effective germicidal activity on the part of d-limonene, but instead states that “d-limonene per se has been found to possess comparatively little germicidal activity.” (Col. 1, lines 62-62). And the fact that limonene, due to its activity as a solvent and penetrant, may enhance the bactericidal activity of true antibacterial agents, does not equate to limonene by itself being an effective bacteriocidal. Applicant’s Claim 1 provides for the application of a formulation comprising d-limonene to the skin the nasal cavity of an animal “for a time sufficient for said d-limonene to effectively eradicate or inhibit the growth of said bacteria.” Greathouse does not teach the use of d-limonene as the compound responsible for this antibacterial activity.

In view of the foregoing, it is respectfully submitted that claim 1 as amended is not anticipated by Greathouse et al. or Chastain et al.

Claim rejections under 35 U.S.C. §102(e):

The Examiner has also maintained her rejection of claims 1, 3, and 5 under 35 U.S.C. §102(e) as being anticipated by Franklin (U.S. Pub. No. 2003/0180349). For the following reasons, the Applicant respectfully traverses this rejection.

It is respectfully submitted that Franklin is an improper prior art reference with respect to the Applicant’s claims. Franklin has a filing date of December 9, 2002, and claims the benefit of the filing date (December 7, 2001) of an earlier filed provisional application. The Applicant has obtained a copy of Franklin’s provisional application (copy attached hereto as Ex. A), and nowhere is there any teaching whatsoever of the use of d-limonene as an antibacterial agent. Consequently, with respect to any teachings of the use of limonene as an antibacterial agent, the

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Franklin reference is only entitled to an effective date of December 9, 2002 as a prior art reference. The Applicant's application, while filed on July 7, 2003, has an effective priority date of July 8, 2002 (SN 60/394,333), and which clearly supports the Applicant's currently pending claims and pre-dates the effective prior date of the Franklin reference (i.e. December 9, 2002) by approximately five months. In view of the foregoing, it is the Examiner's burden to show where there is a disclosure or teaching of the use of d-limonene as an antibacterial agent in the Franklin provisional application. Absent such a teaching, the Applicant respectfully requests that the Franklin published application be withdrawn as a prior art reference against the Applicant's claims.

Conclusion:

In view of the foregoing amendments and remarks, it is respectfully submitted that claim 1 as well as claims 2-5 dependent thereon, are patentable in view of the cited art, and thus withdrawal of the Examiner's rejections is hereby requested.

Respectfully submitted,



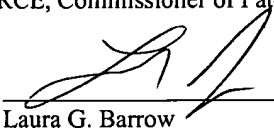
Laura G. Barrow (Reg. No. 35,437)

Date: 12/26/06

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CERTIFICATE UNDER 37 CFR 1.8(a)

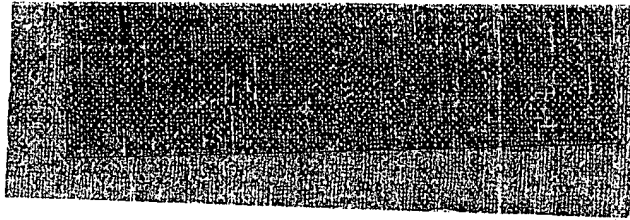
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Laura G. Barrow



	Subclass	ISSUE CLASSIFICATION
	Class	



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Ex A

PROVISIONAL
APPLICATION
NUMBER

Ex A

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INITIALS

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1. Application papers	
2. <i>Report of Case</i>	4-5-08
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FEE DETERMINATION			
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FORMALITY REVIEW	<i>A</i>	<i>676</i>	<i>04/06/02</i>
RESPONSE FORMALITY REVIEW			

PATENT APPLICATION SERIAL NO. _____

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

PTO-1556
(5/87)

*U.S. GPO: 2000-468-987/39595

12/07/01

11054 U.S. PTO

PTO/SB/16 (10-01)

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

INVENTOR(S)

Given Name (first and middle [if any])

Family Name or Surname

Residence
(City and either State or Foreign Country)

LANNY UDELL

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ATLANTA, GA 30342

☐ Additional inventors are being named on the _____ separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

RESPIRATORY INFECTIONS PREVENTION AND TREATMENT

Direct all correspondence to:

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Customer Number

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Individual Name

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ENCLOSED APPLICATION PARTS (check all that apply)



Specification Number of Pages

13



CD(s), Number



Drawing(s) Number of Sheets



Other (specify)



Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT



Applicant claims small entity status. See 37 CFR 1.27.



A check or money order is enclosed to cover the filing fees

FILING FEE
AMOUNT (\$)



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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.



No.



Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

LUFranklin

Date

10.26.01

TYPED or PRINTED NAME

LANNY U. FRANKLIN

REGISTRATION NO.

(if appropriate)

Docket Number:

TELEPHONE

404.822.8906

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C. 20231.

FEE TRANSMITTAL for FY 2002

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT

(\$)
80

Complete if Known

Application Number

Filing Date

First Named Inventor

Examiner Name

Group Art Unit

Attorney Docket No.

LANNY WDELL FRANKLIN

METHOD OF PAYMENT

1. ☐ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

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- ☐ Charge Any Additional Fee Required
Under 37 CFR 1.16 and 1.17
☐ Applicant claims small entity status.
See 37 CFR 1.27

2. ☒ Payment Enclosed:

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Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Small Entity

Fee Fee Fee Fee Fee Description

Code (\$) Code (\$) Code (\$) Code (\$) Code (\$)

101 740 201 370 Utility filing fee

106 330 206 165 Design filing fee

107 510 207 255 Plant filing fee

108 740 208 370 Reissue filing fee

114 160 214 80 Provisional filing fee

Fee Paid

SUBTOTAL (1) (\$)
80

2. EXTRA CLAIM FEES

Extra Claims Fee from below Fee Paid

Total Claims -20** = X =

Independent Claims -3** = X =

Multiple Dependent =

Large Entity Small Entity

Fee Fee Fee Fee Fee Description

Code (\$) Code (\$) Code (\$) Code (\$) Code (\$)

103 18 203 9 Claims in excess of 20

102 84 202 42 Independent claims in excess of 3

104 280 204 140 Multiple dependent claim, if not paid

109 84 209 42 ** Reissue independent claims
over original patent

110 18 210 9 ** Reissue claims in excess of 20
and over original patent

SUBTOTAL (2) (\$)
0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Small Entity

Fee Fee Fee Fee Fee Description

Code (\$) Code (\$) Code (\$) Code (\$) Code (\$)

105 130 205 65 Surcharge - late filing fee or oath

127 50 227 25 Surcharge - late provisional filing fee or
cover sheet

139 130 139 130 Non-English specification

147 2,520 147 2,520 For filing a request for *ex parte* reexamination

112 920* 112 920* Requesting publication of SIR prior to
Examiner action

113 1,840* 113 1,840* Requesting publication of SIR after
Examiner action

115 110 215 55 Extension for reply within first month

116 400 216 200 Extension for reply within second month

117 920 217 460 Extension for reply within third month

118 1,440 218 720 Extension for reply within fourth month

128 1,960 228 980 Extension for reply within fifth month

119 320 219 160 Notice of Appeal

120 320 220 160 Filing a brief in support of an appeal

121 280 221 140 Request for oral hearing

138 1,510 138 1,510 Petition to institute a public use proceeding

140 110 240 55 Petition to revive - unavoidable

141 1,280 241 640 Petition to revive - unintentional

142 1,280 242 640 Utility issue fee (or reissue)

143 460 243 230 Design issue fee

144 620 244 310 Plant issue fee

122 130 122 130 Petitions to the Commissioner

123 50 123 50 Processing fee under 37 CFR 1.17(q)

126 180 126 180 Submission of Information Disclosure Stmt

581 40 581 40 Recording each patent assignment per
property (times number of properties)

146 740 246 370 Filing a submission after final rejection
(37 CFR § 1.129(a))

148 740 248 370 For each additional invention to be
examined (37 CFR § 1.129(b))

179 740 279 370 Request for Continued Examination (RCE)

169 900 169 900 Request for expedited examination
of a design application

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$)
0

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Date

10-26-01

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TITLE OF THE INVENTION

RESPIRATORY INFECTIONS PREVENTION AND TREATMENT

BACKGROUND OF THE INVENTION

Field of the Invention

A method of prevention and treatment of respiratory infections by the inhalation of an aerosol solution containing a single bioactive terpene, a bioactive terpene mixture or a liposome-terpene(s) composition with or without a surfactant.

Discussion of the background

As civilization progresses there has been a tendency to stay longer in closed and confined spaces due to work requirements or for physical comfort. This has resulted in an increase in respiratory problems, especially allergies due to the presence of bacteria, fungi and parasites in these confined places. One of the respiratory problems is sinusitis.

Sinusitis is caused by bacteria (streptococci, staphylococci, pneumococci, Haemophilus influenza), viruses (rhinovirus, influenza virus, parainfluenza virus); and fungi (Aspergillus, Dematiaceae, Mucoraceae, Penicillium sp.)

There are four categories of fungal infections affecting the paranasal sinuses. They are acute or fulminant invasive fungal sinusitis, chronic or indolent invasive fungal sinusitis, fungus ball (mycetoma) and allergic fungal sinusitis. The offending fungi originate from the classes Zygomycetes (Mucor spp.) and Ascomycetes (Aspergillus spp). Chronic sinusitis can develop into granulomatous chronic infection that may extend beyond the sinus walls. Allergic fungal sinusitis colonizes the sinuses of an atopic immunocompetent patient and acts as an allergen, eliciting an immune response. Fungal induced sinusitis most often is seen in immunosuppressed individuals such as those with AIDS, leukemia, lymphoma or multiple myeloma, or in people with poor diabetes control. The Mayo Clinic Proceedings shows a report where 96% out of 210 patients with sinusitis had fungi. Chronic sinusitis last more than 30 days is typically identified by symptoms of a drippy nose, congestion, headaches and reduced sense of smell. Fungal sinusitis is known as eosinophilic fungal rhinosinusitis (EFRS) or eosinophilic mucinous rhinosinusitis (EMRS).

Aspergillus may cause several different illnesses, including both infections and allergy. These fungi may lodge in the airways or a distant part of the lung and grow until they form a compact sphere known as a "fungus ball." In people with lung damage or serious underlying illnesses, *Aspergillus* may grasp the opportunity to invade the lungs or the whole body. In some individuals, exposure to these fungi also can lead to asthma or to a lung disease resembling severe inflammatory asthma called allergic bronchopulmonary aspergillosis. This latter condition, which occurs only in a minority of people with asthma, is characterized by wheezing, low-grade fever, and coughing up of brown-flecked masses or mucus plugs. Skin testing, blood tests, X-rays, and examination of the sputum for fungi can help establish the diagnosis. Corticosteroid drugs are usually effective in treating this reaction. Immunotherapy is not helpful.

Terpenes are widespread in nature, mainly in plants as constituents of essential oils. Their building block is the hydrocarbon isoprene (C_5H_8)_n. Terpenes have been found to be effective and nontoxic dietary antitumor agents which act through a variety of mechanisms of action (Crowell and Gould, 1994 and Crowell et al, 1996). Terpenes, i.e. geraniol, tocotrienol, perillyl alcohol, b-ionone and d-limonene, suppress hepatic HMG-COA reductase activity, a rate limiting step in cholesterol synthesis, and modestly lower cholesterol levels in animals (Elson and Yu, 1994). D-limonene and geraniol reduced mammary tumors (Elegbede et al, 1984 and 1986 and Karlson et al, 1996) and suppressed the growth of transplanted tumors (Yu et al, 1995).

Terpenes have also been found to inhibit the in-vitro growth of bacteria and fungi (Chaumont and Leger, 1992, Moleyar and Narasimham, 1992 and Pattnaik, et al 1997) and some internal and external parasites (Hooser, et al, 1986). Geraniol was found to inhibit growth of *Candida albicans* and *Saccharomyces cerevisiae* strains by enhancing the rate of potassium leakage and disrupting membrane fluidity (Bard, et al, 1988). B-ionone has antifungal activity which was determined by inhibition of spore germination, and growth inhibition in agar (Mikhlin et al, 1983 and Salt et al, 1986). Terpenone (geranylgeranylacetone) has an antibacterial effect on *H. pylori* (Ishii, 1993). Solutions of 11 different terpenes were effective in inhibiting the growth of pathogenic bacteria in in-vitro tests; levels ranging between 100 ppm and 1000 ppm were effective. The terpenes were diluted in water with 1% polysorbate 20 (Kim et al, 1995). Diterpenes, i.e. trichorabdol A (from *R. Trichocarpa*) has shown a very strong antibacterial effect against *H. pylori* (Kadota, et al, 1997).

Rosanol a commercial product with 1% rose oil has been shown to inhibit the growth of several bacteria (*Pseudomona*, *Staphylococcus*, *E. coli* and *H pylori*). Geraniol is the active component (75%) of rose oil. Rose oil and geraniol at a concentration of 2 mg/lt. inhibited the growth of *H pylori* in vitro. Some extracts from herbal medicines have been shown to have an inhibitory effect in *H pylori*, the most effective being decursinol angelate, decursin, magnolol, berberine, cinnamic acid, decursinol and gallic acid (Bae, et al 1998). Extracts from cashew apple, anacardic acid and (E)-2-hexenal, have shown bactericidal effect against *h pylori*. There may be different modes of action of terpenes against microorganism; they could (1) interfere with the phospholipid bilayer of the cell membrane (2) impair a variety of enzyme systems (HMG-reductase) and (3) destroy or inactivate genetic material.

SUMMARY OF THE INVENTION

A method of prevention and treatment of respiratory infections by the inhalation of an aerosol solution contain a single bioactive terpene, a bioactive terpene mixture or a liposome-terpene(s) composition.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Poor air quality is one of the major factors that produce respiratory infections in humans. The presence of microorganisms, toxins and allergens is mainly due to poor ventilation, excess moisture and improper cleaning and disinfection. The present invention has the capacity of reducing the incidences of and treating respiratory infections. This invention is comprised of naturally occurring chemicals that are found in plants and that are generally recognized as safe (GRAS) by the FDA. One of the most important aspects of this invention is that due to the mechanism of action terpenes do not generate microbial resistance. There are antimicrobial products containing terpenes, basically in the form of essential oils, but we have found that not all components of the essential oils are biocides. Another advantage of the present invention is that by varying the concentration of terpenes we can have different specificity and biocidal effect and that combining two or more terpenes in the same solution a synergistic effect can be obtained. Another important property of this invention is that the terpenes and surfactant used are generally recognized as safe (GRAS) by the FDA. Another property of this invention is that we can tailor the formulation and obtain biocidal effect over a single type microorganism or change

the formulation and eliminate all types of microorganisms. Applying one of the formulations of the present invention in spray form into the nasal cavities reduces the amount of microorganism responsible of infections like aspergillius and stachybotrys (fungi). These microorganisms are responsible of the majority of respiratory infections present in immuno-deficient patients and children. Several formulations can be obtained by utilizing biocidal terpenes without departing from the principle of the present inventions. Formulations can vary not only in the concentration of terpenes but also in the type of surfactant used. This invention can be readily be mixed with other types of nasal delivery medications. Another advantage of the present invention is that the terpenes present in the formulation can reach all areas of the respiratory system including the lungs. We have found that higher concentrations of certain terpenes can be irritating to the nasal passages, and that by reducing or eliminating these terpenes in the formulation we still have the benefit of the other terpenes. The terpenes we have used in the present invention include citral, carvone, eugenol, b-ionone. All of them have biocidal properties; and other biocidal terpenes can be utilized without departing from the scope of the present invention.

We have observed that the terpenes used in this invention can be targeted to different microorganisms and parasite, we have been able to prove the effectiveness of the present invention against bacteria, fungi and parasites that are of importance for humans and animals. Also the effective terpene dose varies depending on the organism we are interested in eliminating. This invention can be modified in several ways by adding or deleting from the formulation the type of terpene and surfactant. The surfactant can be non-ionic, cationic or anionic.

It will be apparent for those skilled in the art that the aforementioned objects and other advantages may be further achieved by the practice of the present invention.

EXAMPLE 1: Preparation of the terpene mixture

The terpene, terpene mixture or liposome-terpene(s) combination consists of a blend of generally recognized as safe (GRAS) terpenes with a GRAS surfactant. The ratio of terpenes is from 1-99% and the surfactant ratio from 1-99% of the mixture. The terpenes, comprised of natural or synthetic terpenes, are citral, b-ionone, eugenol, geraniol, carvone, terpeniol, carvacrol, anethole or other terpenes with similar properties. The surfactant is preferably polysorbate-80 or other suitable GRAS surfactants.

EXAMPLE 2: Preparation of the terpene mixture

The terpene-water solution is formulated without a surfactant. 100 ppm to 2000 ppm of natural or synthetic terpenes such as citral, b-ionone, geraniol, carvone, terpeniol, carvacrol, anethole, or other terpenes with similar properties are added to water and subjected to a high-shear blending action that forces the terpene(s) into a true solution. The maximum level of terpene(s) that can be solubilized varies with each terpene.

EXAMPLE 3: In in-vitro effectiveness of terpenes against *Aspergillus fumigatus*

This example demonstrates the effectiveness of the terpene mixture against *Aspergillus fumigatus*. *A. fumigatus* was grown for 48 hours at 25-27 °C in tryptose broth and adjusted to approximately 10^5 organisms/ml with sterile saline. For the broth dilution test, terpene mixture containing citral, b-ionone, carvone, eugenol and surfactant was diluted in sterile tryptose broth to give the following dilutions: 1:500, 1:1000, 1:2000, 1:4000, 1:8000, 1:16,000, 1:32,000, 1:64,000 and 1:128,000. Each dilution was added to sterile tubes in 5-ml amounts. Three replicates of each series of dilutions were used. One half ml of the organism was added to each series and incubated at 25-77 °C for 72 hours. After incubation the tubes were observed for growth and plated onto blood agar. The tubes were incubated an additional 24 hours and observed again. The minimum inhibitory concentration for each test organism was determined as the highest dilution that completely inhibits the organism.

Table 1: Results of the inhibitory activity of different dilutions

Organism	Visual assessment of growth *			Growth after subculture to agar plates *			Mean inhibitory dilution
	1	2	3	1	2	3	
<i>A. fumigatus</i>	8000	16,000	16,000	8000	16,000	16,000	13,300
* The results of the triplicate tests with each organism as the reciprocal of the dilution that showed inhibition/killing							
** NI = not inhibited							

EXAMPLE 4: In-vitro effectiveness of different terpene formulations.

This example shows the amount and types of terpenes from six different terpene formulations (table 2). In the microbiological study seven microorganisms including *Escherichia coli*, *Salmonella typhimurium*, *Pasteurella mirabilis*, *Pseudomona aeruginosa*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus fumigatus* were utilized. These microorganisms were selected in view that they are commonly present in infections and contaminate animal products utilized for human consumption. Each organism, except *A. fumigatus*, was grown overnight at 35-37 °C in tryptone broth. *A. fumigatus* was grown for 48 hours. Each organism was adjusted to approximately 10^5 organisms/ml with sterile saline. Each terpene formulation was diluted to 1:500, 1:1000, 1:2000, 1:4000, 1:8000 and 1:16000 in broth and/or saline. Each terpene formulation dilution was added to sterile tubes in 5-ml amounts and 5 ml of the test organism was added to each series and incubated for 1 hour. There were three replicates of each series of dilutions for each test organism. After incubation half a ml of each tube was plated onto blood agar and incubated 18-24 hours at 35-37 °C. The *A. fumigatus* test series was incubated for 72 hours at 25 °C. The minimum inhibitory concentration for each test organism was determined as the highest dilution that completely inhibits the organism growth. The microbiological results are presented on table 3.

Table 2: Terpene formulation used for antimicrobial testing

	Formulas (%)					
Terpenes	A	B	C	D	E	F
Citral		15			20	70
Carvone			55	55	35	10
Eugenol			35		40	10
B-ionone	30	80	10	40		
Liposome	70					
Tween-80		5	5	5	5	10

Table 3: Effect of different terpene formulations on microorganism growth

Dilution at which microorganism growth was inhibited						
Organism	Formulas					
	A	B	C	D	E	F
<i>E. coli</i>	NI	NI	NI	NI	2000	1000
<i>P. aeruginosa</i>	NI	NI	NI	NI	2000	NI
<i>P. mirabilis</i>	NI	NI	NI	NI	1000	1000
<i>S. typhimurium</i>	NI	NI	NI	NI	2000	500
<i>S. aureus</i>	NI	4000	1000	4000	2000	1000
<i>C. albicans</i>	NI	1000	2000	2000	2000	1000
<i>A. fumigatus</i>	NI	NI	NI	NI	500	13300
The results are expressed as the reciprocal of the dilution that showed biocidal effect. NI not inhibited						

EXAMPLE 4: In in-vitro effectiveness of terpenes against other fungal microorganisms.

Two terpene formulations were tested against *Sclerotinia homeocarpa*, *Rhizoctonia solani* and *Colletotrichum graminicola*. Potato dextrose agar media was amended with each terpene formulation to make a 5000 ppm final concentration of each. For each pathogen, a 5mm-diameter agar plug containing fungal micelia was transferred to each of 5 plates for both terpene formulation and control. All plates were parafilmmed and incubated at 25°C. The diameter of fungal colony growth was measured (mm) and recorded. When the control plates were full, measurements were stopped. Colony area was calculated using πr^2 , where r is the radius of the colony.

Table 4: Effect of terpenes on fungal growth (area mm²)

Treatment	<i>S. homeocarpa</i>		<i>R. solani</i>		<i>C. graminicola</i>	
	Day 1	Day 2	Day 1	Day 2	Day 2	Day 7
Formula "A"	0	0	0	0	0	0
Formula "B"	0	0	0	0	0	0

Control	209.0	2023.2	162.3	1976.6	136.7	2023.2
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EXAMPLE 6: In vitro effectiveness of single or combination of terpenes against E. coli.

The objective of this example was to determine a terpene mixture that could have an optimal biocidal effect. E. coli strain AW574 was grown in tryptone broth to an exponential growth phase (O.D. between 0.4 and 1.0 at 590 nm). One tenth of this growth was inoculated to 10 ml of tryptone broth following by the addition of individual terpenes or as indicated on table 2; then incubated for 24 hours at 35-37 °C and the O.D. determined in each tube. The concentration of terpenes was 1 or 2 uMol. Each treatment was repeated in triplicate. The results are expressed as percentage bacterial growth as compared to the control treatment. It is observed that the combination of terpenes gives better biocidal effect than single terpenes, with geraniol and carvone better than b-ionone.

**Table 5: Effect of single terpene or their combination
against on E. coli growth**

uMol terpenes			% growth
B-ionone	Carvone	Geraniol	
0	0	0	100.00
2	0	0	84.00
0	2	0	63.00
0	0	2	54.00
1	1	1	41.00
1	2	1	31.10
1	1	2	14.80
1	2	2	15.90
2	1	1	48.60
2	2	1	44.30
2	1	2	30.20
2	2	2	1.50

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References

1. Bae EA, MJ Han, NJ Kim and DH Kim, 1998. Anti-Helicobacter pylori activity of herbal medicines. Biol, Pharm. Bull 21(9) 990-992.
2. Bard, M, MR Albert, N Gupta, CJ Guuynn and W Stillwell, 1988. Geraniol interferes with membrane functions in strains of Candida and Saccharomyces. Lipids 23(6): 534-538.
3. Barranx A, M Barsacq, G Dufau and JP Lauilhe, 1998. Disinfectant or antiseptic composition comprising at least one terpene alcohol and at least one bactericidal acidic surfactant, and use of such a mixture. US patent# 5763468.
4. Boyanova L and G Neshev, 1999. Inhibitory effect of rose oil products on Helicobacter pylori growth in vivo: preliminary report. J. Med. Microbiol. 48: 705-706.
5. Chaumont JP and D Leger, 1992. Campaign against allergic moulds in dwellings. Inhibitor properties of essential oil geranium "Bourbon", citronellol, geraniol and citral. Ann Pharm Fr 50(3): 156-166.
6. Crowell, PL and MN Gould, 1994. Chemoprevention and therapy of cancer by d-limonene. Crit Rev Oncog 5(1): 1-22.
7. Crowell, PL, S Ayoubi and YD Burke, 1996. Antitumorigenic effects of limonene and perillyl alcohol against pancreatic and breast cancer. Adv Exp Med Biol 401: 131-136.
8. Elegbede, JA, CE Elson, A Qureshi, MA Tanner and MN Gould, 1984. Inhibition of DMBA-induced mammary cancer by monoterpene d-limonene. Carcinogenesis 5(5): 661-664.
9. Elegbede, JA, CE Elson, A Qureshi, MA Tanner and MN Gould, 1986. Regression of rat primary mammary tumors following dietary d-limonene. J Natl Cancer Inst. 76(2): 323-325.
10. Elson, CE and SG Yu, 1994. The chemoprevention of cancer by mevalonate-derived constituents of fruits and vegetables. J Nutr. 124: 607-614.
11. Hooser, SB, VR Beasley and JJ Everitt, 1986. Effects of an insecticidal dip containing d-limonene in the cat. J Am Vet Med Assoc. 189(8): 905-908.
12. Ishii, E., 1993. Antibacterial activity of teprenone, a non water-soluble antiulcer agent, against Helicobacter pylori. Int. J Med Microbiol Virol. Parasitol. Infect Dis. 280(1-2): 239-243.
13. Iyer LM, JR Scott, and DF Whitfield, 1999. Antimicrobial compositions. US patent# 5,939,050.

ABSTRACT OF THE INVENTION

Prevention and treatment of respiratory infections by the inhalation of a solution containing a single bioactive terpene, a bioactive terpene mixture or a liposome-terpene(s) composition before or after the onset of the infection.

2024-03-28

14. Karlson, J, AK Borg, R Unelius, MC Shoshan, N Wilking, U Ringborg and S Linder, 1996. Inhibition of tumor cell growth by monoterpenes in vitro: evidence of a Ras-independent mechanism of action. *Anticancer Drugs* 7(4): 422-429.
15. Kim J, M Marshall and C Wei, 1995. Antibacterial activity of some essential oil components against five foodborne pathogens. *J Agric Food Chem.* 43: 2839-2845.
16. Koga, J, T Yamauchi, M Shimura, Y Ogasawara, N Ogasawara and J Suzuki, 1998. Antifungal terpene compounds and process for producing the same. US patent# 5,849,956.
17. Iyer LM, JR Scott, and DF Whitfield, 1999. Antimicrobial compositions. US patent# 5,939,050.
18. Mikhlin ED, VP Radina, AA Dmitrossky. LP Blinkova and LG Button, 1983. Antifungal and antimicrobial activity of some derivatives of beta-ionone and vitamin A. *Prikl Biokhim Mikrobiol.* 19: 795-803.
19. Moleyar V and P Narasimham, 1992. Antibacterial activity of essential oil components. *Int J Food Microbiol* 16(4): 337-342.
20. Onawunmi, GO, 1989. Evaluation of the antimicrobial activity of citral. *Letters in Applied Microbiology* 9(3): 105-108.
21. Pattnaik, S, VR Subramanyan, M Bapaji and CR Kole, 1997. Antibacterial and antifungal activity of aromatic constituents of essential oils. *Microbios* 89(358): 39-46.
22. Salt, SD, S Tuzun and J Kuc, 1986. Effects of B-ionone and abscisic acid on the growth of tobacco and resistance to blue mold. Mimicry the effects of stem infection by *Peronospora tabacina*. *Adam Physiol Molec Plant Path* 28: 287-297.
23. Wright, DC, 1996. Antimicrobial oil-in-water emulsions. US Patent #5,547,677.
24. Wright, DC, 1996. Antimicrobial oil-in-water emulsions. US Patent #5,549,901.
25. Wright, DC, 1997. Antimicrobial oil-in-water emulsions. US Patent #5,618,840.
26. Wright, DC, 1997. Micellar nanoparticles. US Patent #5,629,021.
27. Wright, DC, 1997. Oil containing lipid vesicles with marine applications. US Patent #5,662,957.
28. Wright, DC, 1997. Lipid vesicles having a bilayer containing a surfactant with anti-viral and spermicidal activity. US Patent #5,700,679.
29. Wright, DC, 1998. Oral vaccine against gram negative bacterial infection. US Patent #5,730,989.

30. Yu, SG, PJ Anderson and CE Elson, 1995. The efficacy of B-ionone in the chemoprevention of rat mammary carcinogenesis. J Agri Food Chem 43: 2144-2147.

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Filing Date: Dec 07, 2001

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